Contains Nonbinding Recommendations

Draft Guidance on Leuprolide Acetate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Leuprolide Acetate

Form/Route: Injectable/Injection

Recommended studies: 1 study

Type of study: Fasting
Design: Single-dose, randomized, parallel, *in-vivo*
Strength: 7.5 mg/vial
Subjects: Prostatic carcinoma patients undergoing initial therapy.
Additional Comments: The test and reference groups should be balanced with respect to patient disease progression and treatment history. Furthermore, the treatment regimen during the study should be identical between the test and reference groups.

Analytes to measure (in appropriate biological fluid): Leuprolide in serum

Bioequivalence based on (90% CI): Leuprolide

Waiver request of *in-vivo* testing: 3.75 mg/vial, 11.25 mg/vial-1 month, and 15 mg/vial based on: (1) an acceptable bioequivalence study on the 7.5 mg/vial strength (2) acceptable *in vitro* dissolution testing across all strengths and (3) qualitative (Q1) and quantitative (Q2) sameness to the respective RLD strength.

Please note that Leuprolide Acetate for Depot Suspension, 3.75 mg/vial, Leuprolide Acetate for Depot Suspension, 7.5 mg/vial, and Leuprolide Acetate for Depot Suspension, 7.5 mg/vial, 11.25 mg/vial-1 month, and 15 mg/vial are the subject of three separate reference products. For each strength for which a biowaiver is requested, it might be necessary to submit two separate applications comparing to the appropriate reference product.

An applicant may request a waiver of in vivo bioequivalence testing for the 3.75 mg/vial, 7.5 mg/vial, 11.25 mg/vial-1 month, and 15-mg/vial strengths provided that it (1) submits an ANDA containing an acceptable in vivo study on the 7.5-mg/vial strength; (2) if necessary, cross-references the appropriate ANDA for the 7.5-mg/vial strength; and (3) documents Q1 and Q2 sameness to the respective RLD strength. Please refer to the Guidance for Industry, *Variations in Drug Products That May Be Included in a Single ANDA*, located at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072892.pdf.

Dissolution test method and sampling times:

Please note that the **Dissolution Method Database** is available to the public at the OGD website at http://www.accessdata.fda.gov/scripts/cder/dissolution/. Please find the dissolution information for this product at this website. Please conduct comparative dissolution testing on 12 vials each of all strengths of the test and reference products. Specifications will be determined upon review of the application.